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COMPARATIVE EFFECTS OF SINGLE VS. MULTIPLE DOSING OF MARIJUANA ON PSYCHOMOTOR TRACKING PERFORMANCE

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ABSTRACT

A laboratory experiment was conducted to compare the effects of two different marijuana dosing techniques on psychomotor tracking performance. Most experimental research into the effects of marijuana on driver behavior, including laboratory, simulator and closed course studies, have used the single dose technique, in which the prescribed dose is prepared as a single cigarette and smoked all at once. However, in a typical social setting, marijuana is smoked over much longer periods, often as long as two hours or more. This experiment was performed to determine whether smoking marijuana in an extended rather than a compressed period might have a differential effect on performance.

Fourteen young, experienced male users were treated with marijuana and then tested on the Critical Tracking Task and the Tracometer. The psychomotor tests were given immediately after treatment as well as three hours later. Each subject received both treatments, about one week apart.

Both tracking tasks were found to be sensitive to the effects of marijuana, though only the Tracometer was sensitive to the difference in dosing technique. The multiple dose technique appeared to produce greater impairment than did the single dose technique. These results suggest that most previous research in this area may have underestimated the effects of marijuana due to the use of the single dose technique. It would, therefore, be prudent in future experiments into the effects of marijuana on human performance to administer the drug in a manner which more closely parallels its social use in order to assure greater validity of the results.

INTRODUCTION

The research reported in this paper was performed as a pilot study for a large closed-course study of the effects of marijuana and alcohol on driving. In the field study it was proposed to administer the marijuana dose in the form of several small cigarettes distributed over an extended period of two hours, in contrast to the traditionally-used laboratory method in which the dose is administered in a single cigarette and consumed in a ten to twenty minute period. This multiple dose technique was considered more ecologically valid since it more closely parallels the social use of this drug. Previous experimental research into the effects of marijuana on driving behavior, including laboratory, simulator and closed-course studies, have typically used the single dose technique (1, 2, 3, 4, 5, 6, and 7). Consequently, it was important to determine whether there are differential effects which might arise from the use of a different dosing technique and, in particular to what extent the findings of the proposed field study can be compared with previous research. There appeared to be no relevant previous research on this issue.

To address this question, a laboratory experiment was designed to compare the effects of two dosing techniques on psychomotor tracking performance. In addition, since one of the objectives of the closed-course study (for which this study was a pilot) was to examine the effects of marijuana on driving the morning after consumption, as well as immediately after, the psychomotor tests were given during two testing sessions; immediately following the dosing period as well as three hours later. The marijuana dose level used, 200 mcg THC per kilogram bodyweight, was the maximum dose proposed for the closed-course study.

EXPERIMENTAL PROCEDURES

Experimental Design:

The experimental design was a within subject, 1-way counterbalanced design. Each subject was treated with marijuana on two separate occasions, using different techniques. In order to control for order effects, half of the subjects received the multiple dose technique first and the other half received the single dose technique first. On each occasion, the subject received a dose level of 200 mcg THC per kg bodyweight and then performed two sessions of psychomotor tests. The test sessions, consisting of trials on the Critical Tracking Task and the Tracometer, were given immediately folowing treatment and repeated three hours later.

Subjects:

Fourteen male subjects were selected from respondants to newspaper advertisements. To qualify, subjects had to be 19-30 years old and to have used marijuana at least once every 2 weeks and at most 4 times weekly. The Minnesota Multiphasic Personality Inventory was used to screen out subjects with potential underlying psychological difficulties which could result in severe negative emotional reactions under stress or under the influence of marijuana. Medical examinations were used to eliminate individuals who were not in good health or who were under medication.

Test Battery:

The behavioural test battery consisted of two psychomotor tests; the Critical Tracking Task (CTT) and the Tracometer. Both of these tests measure tracking ability and have previously been used to study the effects of drugs on behaviour, (eg. 8 and 9).

The Critical Tracking Task is a closed-loop compensatory tracking task in which the dynamics of the controlled element are inherently unstable, (10). The equipment set-up is shown in Figure 1. A bright horizontal line is displayed to the subject on a cathode ray tube. At the start of a trial the line begins to move erratically about the centre position and the subject's task is to maintain it at the centre using a joy stick. The subject's task is made more difficult with time through software control of the control-display dynamics such that eventually the line can no longer be controlled and goes off the screen. Klein and Jex (10) suggest as an analogy the balancing of a long stick on one's finger, where the length of the stick decreases with time. When the stick is long it is easy to balance but as it gets shorter the task becomes more difficult. The difficulty level at which

it goes off the screen, known as the "critical instability level" (λ), represents the maximum performance limit for that subject and is a single value derived from the model parameters. This critical instability level (λ) approximates the reciprocal of the operator's effective time delay. Previous studies which have investigated the sensitivity of this task to drug effects have shown significant decrements in performance under alcohol (8 and 10) and marijuana (11) intoxication.

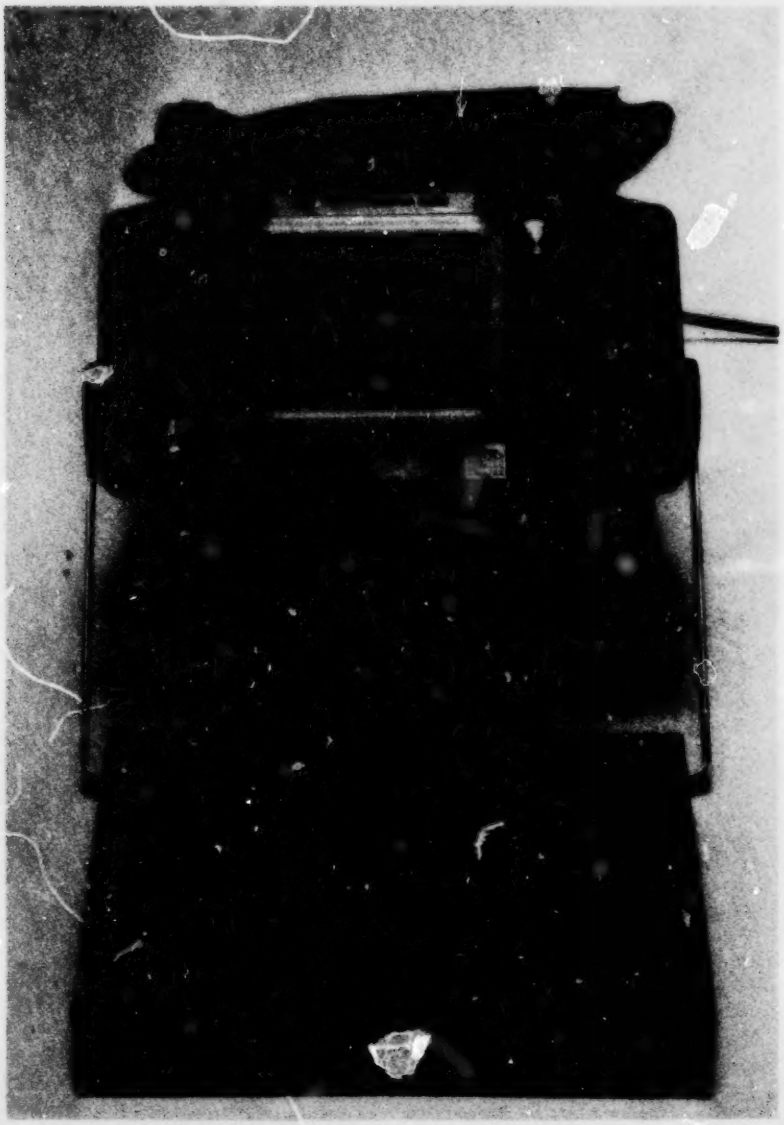

FIGURE 1: Critical Tracking Task

The Tracometer (previously known as the Stressalyzer), is a step-input, subject-paced pursuit tracking task. The Tracometer is shown in Figure 2. The subject is seated in front of a display consisting of five small target lights, arranged in an arc. Only one light is illuminated at any given moment. The trial begins with the centre light illuminated and the pursuit pointer slightly off-centre. The subject's task is to align the pursuit pointer with the target by rotating the control wheel away from the target. When the subject has it accurately aligned for 200 msec., that target is extinguished and a new one appears at one of the other four positions. The subject continues to chase the target from its first appearance, as it makes 100 movements, apparently at random, between the five positions.

The Tracometer provides measures of reaction time, movement time, error score and overshoot score as well as total response time to complete the 100 movements. Several investigations have shown that these measures are sensitive to such factors as sleep loss (12), alcohol (9), (13) and insulin-induced hypoglycaemia (14) demonstrating the usefulness of the device in examining behavioral impairment. An analysis of drug effects on the individual component measures provided by the Tracometer can be used to determine which underlying cognitive mechanisms are being affected and how. For a more detailed description of the Tracometer see (15).

FIGURE 2: Tracometer

Drug Administration:

Each subject received 200 mcg of delta-9 THC per kilogram bodyweight. The purity of the marijuana was assayed at 1.54% delta-9 THC. For the single dose technique the total dose was divided into two parts and rolled as two cigarettes which were smoked one immediately after the other. The amount of marijuana was simply too large to roll into one cigarette. For the multiple dose technique the dose was divided into four equal parts and rolled as four cigarettes which were smoked at the rate of one every half hour.

Each cigarette contained two 1 cm placebo plugs, one at each end. Two marks were drawn on the cigarette paper to indicate the location of the placebo plugs. The plug at the burning end helped to minimize dosage losses due to lighting. At the inhalation end, the plug served as a butt and used to secure the marijuana cigarette in a short glass tube. The glass holder cooled the smoke and allowed the entire cigarette to be smoked. Subjects were instructed to allow the cigarette to burn to the first mark before inhaling any of the smoke. The cigarette was considered to be completely consumed when it had burned to the second mark. The marijuana was administered in a room which had been furnished to simulate a 'home' environment.

Training Schedule:

One week prior to the first treatment session, subjects received about two and a half hours of training on the performance tasks. Subjects completed 75 trials on the Critical Tracking Task in blocks of 15 with short pauses in between. Performance on the Critical Tracking Task has been shown to asymptote at about 50 trials, (11). Subjects also completed 16 trials on the Tracometer in blocks of 4 with short rest pauses in between. Performance on the Tracometer has been shown to asymptote at about 16 trials, (16).

In order to avoid massed practice effects, subjects alternated between tests, receiving half of the training trials on the Critical Tracking Task, switching to the Tracometer, and so on. During training, subjects received feedback at the end of every trial and were encouraged to improve their performance.

Testing Schedule:

Subjects were asked to abstain from all drug use during the course of this study and not to consume any alcoholic beverages 24 hours before each treatment session. Two subjects were treated on each day. Upon arrival at the treatment sessions, each subject was asked to provide a urine sample which was screened for the presence of drugs. Each subject was then administered his marijuana dosage using either the multiple or single dose technique. For both techniques, the puff cycle was the same,

each puff being coached by a research assistant. The puff cycle was as follows: 2 seconds inhale smoke into the mouth and throat, 2 seconds wash into lungs, 4 seconds hold, 2 seconds exhale and 50 seconds rest. This cycle was repeated until the subject had consumed the entire prescribed dose; that is, until the burning end reached the second mark on the cigarette paper.

The difference between techniques was simply a difference in the treatment period; the dose and the puff cycle were constant. For the single dose technique the subject smoked 2 cigarettes each containing 100 mcg THC per kg bodyweight, one after the other. The total smoking time for this technique was approximately 15 minutes. For the multiple dose technique, the subject smoked four cigarettes, each cigarette containing 50 mcg/kg bodyweight THC. The time interval between cigarettes was 30 minutes; hence the full dose for this technique was administered over a period of two hours.

Fifteen minutes after the total dose was consumed, the subject had a blood draw. The subject was then taken to the test room where he began the first test session. The test session consisted of 5 trials on the Tracometer followed by a five minute break and then 25 trials on the Critical Tracking Task. The first trial on the Tracometer and the first 5 trials on the Critical Tracking Task were considered to be warm-up trials and therefore were not included in the analyses. Following this first test session, the subject received lunch, and completed a questionnaire concerning his subjective impressions of the marijuana dose he had been given. Three hours after the initial set of tests, the testing was repeated. At the conclusion of the second session the subject was driven home. It should be noted that during this experimental process, subjects were not allowed to smoke tobacco or to drink any caffeinated beverages.

The time of day in which testing occurred was the same for both the single and multiple dose conditions in order to control for possible effects of circadian rhythm.

RESULTS

All data analyses were performed using the BMDP statistical package (revised version, December, 1979). Blood data results are not available due to equipment problems which arose during the extraction and derivatization process.

Order Effects:

To test whether there were any effects due to the order in which the treatments were administered an analysis of covariance was run for both the Tracometer and Critical Tracking Task data. The subjects were divided into two groups: those receiving the multiple dose treatment first and those receiving the single dose treatment first. Performance measures from the last training run of each subject were used as covariates. There were no significant group effects for either perfomance test. Consequently the data were then combined and analyzed as a within-subject, one-way counterbalanced design with 14 subjects.

Test Sensitivity to Marjuana Effects:

Figures 3 and 4 present the multiple and single dose performance levels, λ , for the Critical Tracking Task and the total response time for the Tracometer respectively. It is evident that for both tests, there was a marked decrement in performance relative to baseline values. The last blocks of training data on the Critical Tracking Task (4 trials) and the Tracometer (4 trials) were used as the baseline values for each subject. From Figures 3 and 4 it is also evident that, for both tests, there was a significant recovery three hours later.

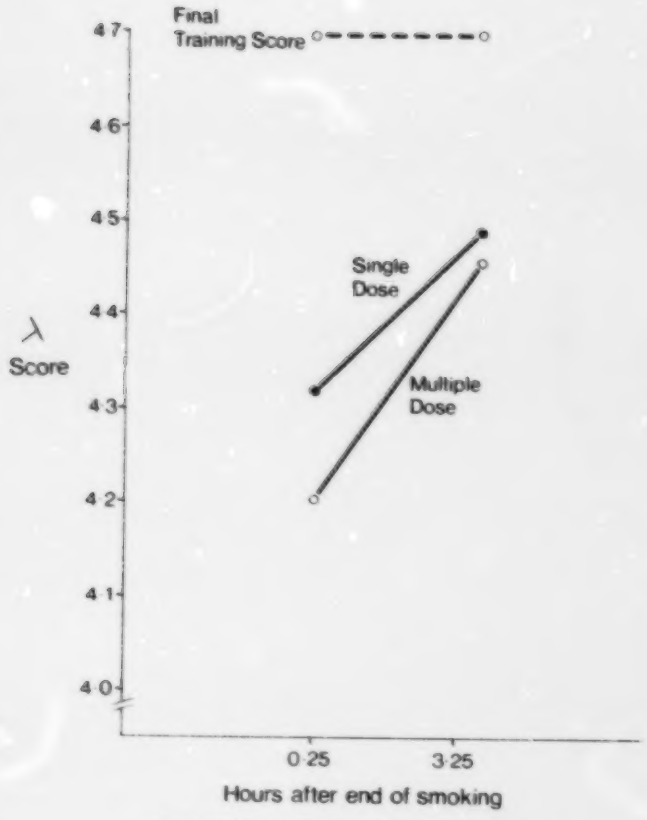

Fig.3 Critical Tracking Task Score

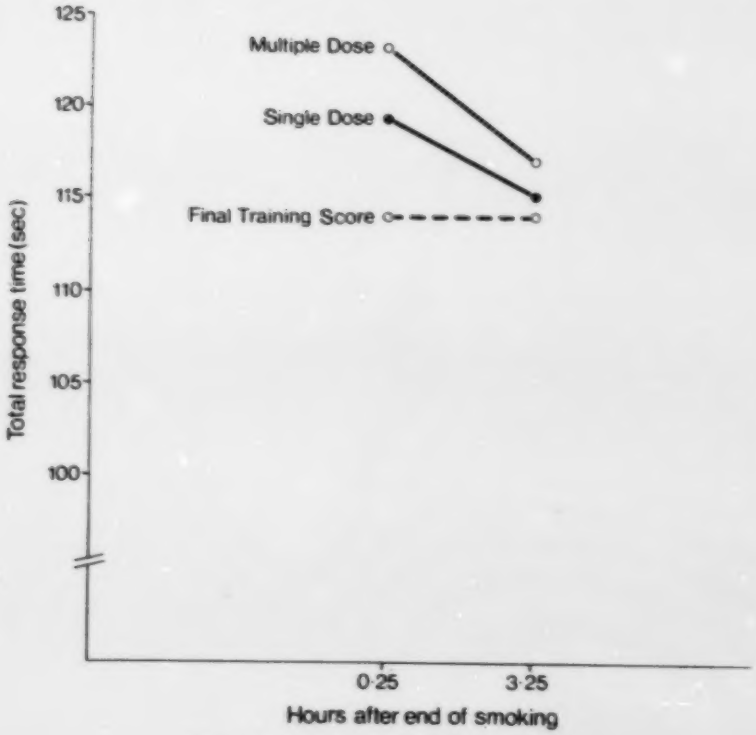

Fig. 4 Total Response Time: Tracometer

To test the statistical significance of these effects, an analysis of variance was run using the end of training data as baseline levels. This was considered to be a conservative test since there may have been some further learning after the end of training. Nonetheless, from Table 1 it can be seen that both the Critical Tracking Task and the Tracometer were sensitive to the effects of marijuana. The score obtained on the Critical Tracking Task was significantly lower after both the single and multiple dose treatments when compared to the training runs ($p < 0.03$, $p < 0.007$ respectively). Similarly, the total response time on the Tracometer was longer after the multiple dose treatment when compared to the last 4 training runs ($p<0.001$), and after the single dose treatment as well ($p<0.07$). The total response time is a global measure which includes reaction time, movement time and delays due to errors (starting off from a target in the wrong direction) and due to overshoots (going past the target and having to return to it). From Table 1, it appears that the increase in total response time with treatment appeared to be mainly due to an increase in movement time (overshoots not included) and an increase in average overshoot score.

Table 1. Summary of Means and P-Values for Training vs Active Treatment.

	Means			p Values	
	train	single	multiple	train vs single	train vs mult.
CTT mean score	4.70	4.32	4.20	0.029	0.007
TRACOMETER					
total response time sec.	114	119	123	0.070	0.001
avg. non-overshoot movement time msec.	765	777	807	0.150	0.003
avg reaction time msec	293	286	286	NS	NS
avg over-shoot score %	39.5	46.5	44.2	0.0007	0.018
avg error score %	28.0	27.5	28.5	NS	NS

Single vs Multiple Dose Treatments:

Table 2 shows the results of analyses of variance on the Critical Tracking Task measure (λ) and five Tracometer measures. This table permits comparisons to be made of the sensitivity of these measures to differences between the single and multiple dose treatments. The Critical Tracking Task, though sensitive to the overall drug effect (see Table 1) was not sensitive to differences between the dosing techniques. The Tracometer however did show a small but highly significant treatment effect. Total response time was significantly longer for the multiple dose treatment ($p < 0.005$). Performance had significantly improved three hours after the end of smoking ($p < 0.003$), however the performance after the multiple dose treatment was still poorer than after the single dose. Though differences due to treatment for the individual Tracometer measures did not reach significance at the 0.05 level, the means shown in Table 2 suggest that increases in movement time (overshoots not included) and in error score under the multiple dose treatment were the main contributors to the larger total response time. Figures 5 and 6 illustrate the effects of the treatments on movement time and error rate, the two most affected components of the total response time.

Table 2: Single Dose vs Multiple Dose Treatment.

		Means		P values		
		single	multiple	treatment	period	treatXper
CTT mean score	t=0.25hr	4.32	4.20	NS	NS	NS
	t=3.25hr	4.49	4.46			
TRACOMETER						
total response	t=0.25hr	119	123	0.005	0.003	NS
time (msec)	t=3.25hr	115	117			
avg movement	t=0.25hr	777	807	NS	0.073	0.056
time (msec)	t=3.25hr	763	766			
avg reaction	t=0.25hr	286	286	NS	0.060	NS
time (msec)	t=3.25hr	275	276			
avg overshoot	t=0.25hr	46.5	44.2	NS	NS	NS
rate	t=3.25hr	46.1	45.2			
avg error	t=0.25hr	27.5	28.5	0.092	NS	NS
rate	t=3.25hr	26.1	28.7			

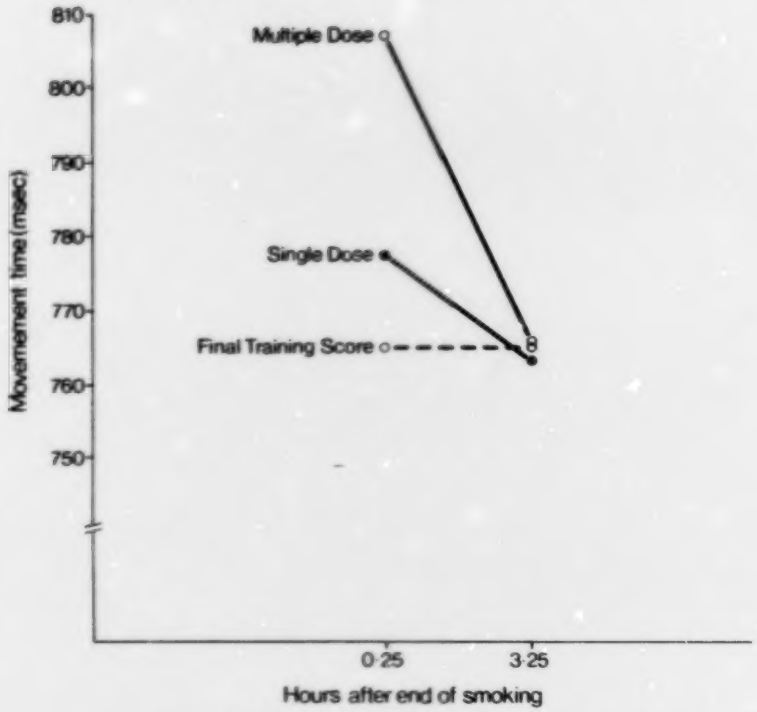

Fig. 5 Average Movement Time Tracometer
(overshoots not included)

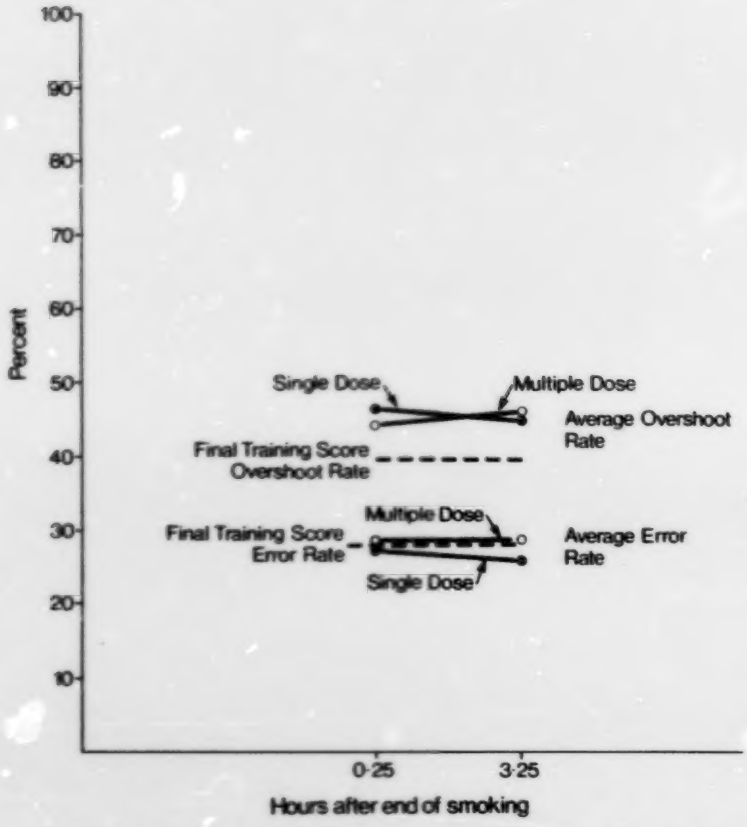

Fig. 6 Average Overshoot Rate and Average Error Rate: Tracometer

Subjective Questionnaire:

Subjects reported very similar subjective reactions to both dosing techniques. The following is a summary of the response patterns for the post-treatment questionnaire, for both multiple and single dose techniques:

* they thought they did poorly to fair on the performance tasks;
* they felt strongly affected by the dose;
* they experienced somewhat worse concentration;
* they did not experience any alterations in their perceptions of time;
* they felt somewhat better after smoking the marijuana;
* they reported getting at least that high on half of the occasions when they smoke marijuana;
* they felt they would normally consume the same dose over a two-hour period; and,
* they reported driving once or twice a year after having a similar dose.

All subjects felt that the puff cycle (ie. inhale, wash, hold, rest) was satisfactory. There were no meaningful differences in their responses due to dosing technique.

DISCUSSION

The concentration of THC in the blood is known to peak within minutes of smoking and to decay very rapidly thereafter. This would suggest that the single dose treatment should produce higher blood levels of THC at the time of testing than the multiple dose treatment. However, the multiple dose treatment appeared to produce greater impairment, suggesting that the behavioural effects of marijuana do not necessarily correlate well with the concentration of THC in the blood. Rather more important is the concentration of THC at the active site in the brain (as yet unknown). Therefore, a possible explanation for these results is that the multiple dose technique allows time for the concentration of the active agent to reach higher levels at the active site, thereby producing larger initial impairment.

The Tracometer appeared to be more sensitive than the Critical Tracking Task to the differences between dosing techniques but generally less sensitive to the marijuana. The explanation for this may lie in the fact that the data from the training runs were used as baseline measures to test for sensitivity to marijuana. Subjects received relatively more training on the Critical Tracking Task than on the Tracometer, in comparison with learning data reported in previous studies (Sharma, 1975; Buck et al, 1978). It is conceivable that learning on the Tracometer may not have plateaued at the end of training. Hence, the Tracometer may not have been as sensitive to the effects of marijuana as the Critical Tracking Task because of performance improvements due to learning. However, because the treatment order was counterbalanced, learning would not be expected to affect the sensitivity of the task to the difference between techniques. Thus the amount of learning on each task affects its sensitivity to the marijuana treatment but has no effect on finding a difference between administration techniques.

The findings of this study suggest that the single dose method normally used in experiments of this nature may underestimate the effect of marijuana on driving. The multiple dose method produced higher decrements in performance, for the given dose. Though the multiple dose technique may be more time-consuming, it is certainly more ecologically valid. More important, it does appear to produce different, perhaps more relevant, results than the single dose method for experimental research into the effects of marijuana on human performance.

CONCLUSIONS

Both the Critical Tracking Task and the Tracometer were sensitive to the effect of the marijuana. Only the Tracometer, however, was sensitive to differences between the single dose treatment and the multiple dose treatment. Though the absolute differences were small the multiple dose treatment was significantly more impairing as shown by the increased total response time due to increased movement time and increased error rate. The reason for the greater impairment after multiple dosing over an extended period was thought to be due to greater THC levels at the receptor site in the brain.

The findings of this study suggest that the single dose method normally used in experiments of this nature may underestimate the effect of marijuana on driving. It would be prudent in future experiments into the effects of marijuana on human performance to administer the drug in a manner which more closely parallels its social use in order to assure greater validity of the results.

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